

Application Number: 10/810,296. Art Unit: 1631. Reply to Office Action of 02/27/07

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (Original): A multiparameter method of screening for the diagnosis, the prevention or the treatment of atherosclerosis-related coronary heart disease (CHD) or stroke comprising;

defining the disease as atherosclerosis-related CHD or stroke;

defining the normal as free from said disease;

defining the following parameters as atherosclerotic parameters consisting of c = the Low-density lipoprotein (LDL) concentration parameter in mg/dL or c = the C-reactive protein (CRP) concentration parameter in mg/L, p = the blood systolic pressure parameter in mmHg or p = the blood diastolic pressure parameter in mmHg, f = the heart rate parameter in  $s^{-1}$ , a = the radius parameter along arterial radius in cm, T = the temperature parameter of

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blood plasma in °C,  $\alpha$  = the angle parameter between gravity and the mean velocity of blood fluid in arterial vessels in degree and  $z$  = the axial position parameter of diffusional flux along the inner wall in the axial direction of arterial vessels in cm, called diffusional length;

an individual having the measured values of said atherosclerotic parameters of the following expressions:

$$J = A c^{\frac{11}{9}} (v^3 D^{16})^{\frac{1}{27}} \left( \frac{g \cos \alpha + fu}{z} \right)^{\frac{2}{9}} \quad (1.1)$$

or

$$J = B c^{\frac{11}{9}} p^{\frac{1}{3}} T^{\frac{16}{27}} a^{\frac{2}{3}} f^{\frac{2}{9}} z^{-\frac{2}{9}} \quad (1.2)$$

and

$$J = E c^{\frac{11}{9}} D^{\frac{16}{27}} z^{-\frac{2}{9}} (\cos \alpha)^{\frac{2}{9}} \quad (1.3)$$

wherein  $J$  = the mass transfer flux in  $10^{-5}$  g/(cm<sup>2</sup>s),  $A$ ,  $B$  and  $E$  = the constants of conversion factors,  $v$  = the eddy velocity of blood fluid in arterial vessels in cm/s,  $u$  = the mean velocity of the blood fluid in cm/s,  $D$  = the diffusion coefficient in cm<sup>2</sup>/s, and  $g$  = the gravitational acceleration in cm/s<sup>2</sup>;

the individual having the normal values of said

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atherosclerotic parameters;

determining the disease risks yielded by the differences between said measured values and said normal values of said atherosclerotic parameters;

adding all said disease risks together yields a total risk of said disease;

determining a disease risk level containing said total risk of said disease;

selecting an atherosclerotic risk factor related to an atherosclerotic parameter that is the greatest contribution to said total risk of said disease so as to result in said risk factor as a primary therapy target of said disease;

selecting a greater flux between the LDL mass transfer flux and the monocyte mass transfer flux so as to result in said greater flux as a primary cause in said disease;

selecting a greater concentration level between the LDL level in serum and the CRP level in

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blood plasma so as to result in said greater level as a secondary therapy target of said disease;

determining a relative ratio between currently said total risk and previously said total risk so as to yield said relative ratio as a therapeutic efficacy of said disease;

repeating above-mentioned said methods until said disease risk level is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke; and

above-mentioned said methods are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said methods and to output a result of said methods to a display or a memory or another computer on a network, or to a user.

Claim 2 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said LDL concentration parameter, said

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method comprising the steps of:

a measured value,  $c_m$  in mg/dL, of the individual's LDL concentration in human serum is determined using a medical technique for measuring the concentration of blood constituents or said  $c_m$  is determined by the physician;

a normal value,  $c_n$  in mg/dL, of said LDL concentration is determined by the physician or said  $c_n = 100$  mg/dL for adult;

substituting said  $c_m$  and said  $c_n$  into the following expression where  $c_m \geq c_n$ :

$$R_1 = \left( \frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1 \quad (1)$$

and

calculating (1) yields said disease risk  $R_1$  caused by said LDL concentration parameter related to the atherosclerotic risk factors being an elevated LDL concentration in human serum, high-fat diet, hypercholesterolemia or other risk factors that increase said LDL concentration.

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Claim 3 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said CRP concentration parameters, said method comprising the steps of:

a measured value,  $c_m$  in mg/L, of the individual's CRP concentration in human blood plasma is determined using a medical technique for measuring the concentration of blood constituents or said  $c_m$  is determined by the physician;

a normal value,  $c_n$  in mg/L, of said CRP concentration and an equivalent factor, F, are determined by the physician wherein  $F = \left(\frac{D_c}{D_L}\right)^{\frac{16}{27}}$ ,  $D_c$  = the CRP diffusion coefficient and  $D_L$  = the LDL diffusion coefficient or said  $c_n = 1.0$  mg/L for adult and said  $F = 0.66$ ;

substituting said  $c_m$ , said  $c_n$  and said F into the following expression where  $c_m \geq c_n$ :

$$R_2 = F \left( \left( \frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1 \right) \quad (3)$$

and

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calculating (3) yields said disease risk  $R_2$  caused by said CRP concentration parameter related to the atherosclerotic risk factors being an elevated CRP level in human blood plasma, systemic inflammation, infectious agents or other risk factors that increase said CRP level.

Claim 4 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said blood systolic pressure parameter, said method comprising the steps of:

a measured value,  $p_m$  in mmHg, of the individual's blood systolic pressure is determined using a medical technique for measuring the human blood pressure or said  $p_m$  is determined by the physician;

a normal value,  $p_n$  in mmHg, of said systolic pressure is determined by the physician or said  $p_n = 120$  mmHg for adult;

substituting said  $p_m$  and said  $p_n$  into the following expression where  $p_m \geq p_n$ :

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$$R_4 = \left( \frac{P_m}{P_n} \right)^{\frac{1}{3}} - 1 \quad (4)$$

and

calculating (4) yields said disease risk  $R_4$  caused by said systolic pressure parameter related to the atherosclerotic risk factors being an elevated level of blood systolic pressure, family history of hypertension or other risk factors that increase said systolic pressure.

Claim 5 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said blood diastolic pressure parameter, said method comprising the steps of:

a measured value,  $p_m$  in mmHg, of the individual's blood diastolic pressure is determined using a medical technique for measuring the human blood pressure or said  $p_m$  is determined by the physician;

a normal value,  $p_n$  in mmHg, of said blood diastolic pressure is determined by the physician or said  $p_n = 70$  mmHg for adult;

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substituting said  $p_m$  and said  $p_n$  into the following expression where  $p_m \geq p_n$ :

$$R_s = \left( \frac{P_m}{P_n} \right)^{\frac{1}{3}} - 1 \quad (5)$$

and

calculating (5) yields said disease risk  $R_s$  caused by said diastolic pressure parameter related to the atherosclerotic risk factors being an elevate level of blood diastolic pressure, family history of hypertension or other risk factors that increase said diastolic pressure.

Claim 6 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said heart rate parameter, said method comprising the steps of:

a measured value,  $f_m$  in  $s^{-1}$ , of the individual's heart rate is determined using a medical technique for measuring the human heart rate or said  $f_m$  is determined by the physician;

a normal value,  $f_n$  in  $s^{-1}$ , of said heart rate is determined by the physician or said  $f_n = 72$  per

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minute for adult;

substituting said  $f_m$  and said  $f_n$  into the following expression where  $f_m > f_n$ :

$$R_6 = \left( \frac{f_m}{f_n} \right)^{\frac{2}{5}} - 1 \quad (6)$$

and

calculating (6) yields said disease risk  $R_6$  caused by said heart rate parameter related to the atherosclerotic risk factors being an elevated level of heart rate, smoking cigarette, depression or other risk factors that increase said heart rate.

Claim 7 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said arterial radius parameter, said method comprising the steps of:

a measured radius value,  $a_m$  in cm, of the individual's arterial vessel at the lesion-prone sites of arterial bifurcations, arterial branching, arterial curvatures or arterial tapering is determined using a medical technique for measuring the sizes of arterial

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vessels or said  $a_m$  is determined by the physician;

a normal value,  $a_n$  in cm, of said arterial radius is determined by the physician or said  $a_n = a$  value between 0.2 cm and 2.2 cm for adult;

substituting said  $a_m$  and said  $a_n$  into the following expression where  $a_m \geq a_n$ :

$$R_s = \left( \frac{a_m}{a_n} \right)^{\frac{2}{3}} - 1 \quad (7)$$

and

calculating (7) yields said disease risk  $R_s$ , caused by said arterial radius parameter related to the atherosclerotic risk factors being an increased size of arterial radius at said lesion-prone sites or other risk factors that increase the size of said arterial radius.

Claim 8 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said plasma temperature parameter, said method comprising the steps of:

a measured temperature value,  $T_m$  in °C, of the

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individual's plasma fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the temperature of human blood plasma or said  $T_m$  is determined by the physician;

a normal value,  $T_n$  in °C, of said plasma temperature is determined by the physician or said  $T_n = 37^\circ\text{C}$ ;

substituting said  $T_m$  and said  $T_n$  into the following expression where  $T_m \geq T_n$ :

$$R_s = \left( \frac{T_m}{T_n} \right)^{\frac{16}{27}} - 1 \quad (8)$$

and

calculating (8) yields said disease risk  $R_s$  caused by said plasma temperature parameter related to the atherosclerotic risk factors being an elevated temperature of said human blood plasma at said lesion-prone sites, elevated body temperature-related diseases or other risk factors that increase said plasma temperature.

Claim 9 (Original): A method as in claim 1 wherein determining said disease risk yielded by the

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difference between the measured value and the normal value of said angle parameter, said method comprising the step of:

a measured value,  $\alpha_m$  in degree, of the angle between gravity and the average velocity of the blood fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said  $\alpha_m$  is determined by the physician;

a normal value,  $\alpha_n$  in degree, of said angle is determined by the physician or said  $\alpha_n =$  a value between the  $10^\circ$  and  $60^\circ$  for adult;

substituting said  $\alpha_m$  and said  $\alpha_n$  into the following expression where  $\alpha_n \geq \alpha_m$ :

$$R_9 = \left( \frac{\cos \alpha_m}{\cos \alpha_n} \right)^{\frac{2}{9}} - 1 \quad (9)$$

and

calculating (9) yields said disease risk  $R_9$ , caused by said angle parameter related to the atherosclerotic risk factors being a reduced size of said angle or other risk factors that reduce said angle size.

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Claim 10 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said axial position parameter of the diffusional flux, said method comprising the steps of:

a measured value,  $z_m$  in cm, of the individual's axial position of diffusional flux along the inner arterial wall at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said  $z_m$  is determined by the physician;

a normal value,  $z_n$  in cm, of said axial position is determined by the physician or said  $z_n =$  a value between 0.10 cm and 1.00 cm;

substituting said  $z_m$  and said  $z_n$  into the following expression where  $z_m \leq z_n$ :

$$R_{10} = \left( \frac{z_n}{z_m} \right)^{\frac{2}{9}} - 1 \quad (10)$$

and

calculating (10) yields said disease risk  $R_{10}$  caused by said axial position parameter related to the atherosclerotic risk factors being a

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decrease in said axial position of the diffusional flux or other risk factors that decrease said axial position.

Claim 11 (Currently amended): A method as in claim 1 wherein having said nine atherosclerotic parameters-caused nine disease risks and adding said R<sub>4</sub> in claim 2 through said R<sub>10</sub> in claim 10 all nine disease risks together so as to yields yield a total risk of said disease consisting;

a current total risk of said disease related to the currently measured values of said atherosclerotic parameters; and

a previous total risk of said disease related to the previously measured values of said atherosclerotic parameters.

Claim 12 (Currently amended): A method as in claim 1 wherein having said total risk of said disease and determining said disease risk level containing said total risk of said disease in claim 11, said method comprising the steps of:

dividing the disease risk level into the following seven risk sublevels: 0.84 ≥ first

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disease risk level  $\geq 0.00$ ,  $1.75 \geq$  second disease risk level  $> 0.84$ ,  $2.70 \geq$  third disease risk level  $> 1.75$ ,  $3.70 \geq$  fourth disease risk level  $> 2.70$ ,  $4.70 \geq$  fifth disease risk level  $> 3.70$ ,  $5.80 \geq$  sixth disease risk level  $> 4.70$  and seventh disease risk level  $> 5.80$ ; and

selecting a disease risk level containing said total risk of said disease ~~in claim 11~~ from among seven of said disease risk sublevels.

Claim 13 (Currently amended): A method as in claim 1 ~~wherein having said total risk of said disease and~~ selecting an atherosclerotic risk factor related to the atherosclerotic parameter ~~that is~~ ~~having~~ the greatest contribution to said total risk of said disease ~~in claim 11~~ so as to result in said risk factor as a primary therapy target of said disease.

Claim 14 (Currently amended): A method as in claim 1 ~~wherein having said LDL concentration parameter-caused the disease risk R<sub>1</sub> and said CRP concentration parameter-caused the disease risk R<sub>2</sub> and~~ selecting said greater flux between said LDL mass transfer flux and said monocyte mass transfer flux so

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as to result in said greater flux as a primary cause in said disease, said method comprising the steps of:

selecting said LDL mass transfer flux as a primary cause in said disease when said  $R_1 \in$  ~~claim 2~~  $\geq$  said  $R_2$  ~~in claim 3~~; or

selecting said monocyte mass transfer flux as a primary cause in said disease when said  $R_1 \in$  ~~claim 2~~  $<$  said  $R_2$  ~~in claim 3~~.

Claim 15 (Currently amended): A method as in claim 1 ~~wherein having said LDL concentration parameter-caused the disease risk  $R_1$  and said CRP concentration parameter-caused the disease risk  $R_2$~~  and selecting said greater concentration level between said LDL level in human serum and said CRP level in human blood plasma so as to result in said greater level as a secondary therapy target, said method comprising the steps of:

selecting said LDL level in serum as a secondary therapy target of said disease when said  $R_1 \in$  ~~claim 2~~  $\geq$  said  $R_2$  ~~in claim 3~~; or

selecting said CRP level in blood plasma as a secondary therapy target of said disease when

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said R<sub>1</sub> in claim 2 < said R<sub>2</sub> in claim 3.

Claim 16 (Currently amended): A method as in claim 1 wherein having said current total risk of said disease and said previous total risk of said disease and determining said relative ratio between said current total risk of said disease and said previous total risk of said disease ~~in claim 11~~ so as to yield said relative ratio as a therapeutic efficacy of said disease.

Claim 17 (Currently amended): A method as in claim 1 wherein ~~repeating said method in claim 2 through said method in claim 16 all the methods in said all processes in claim 1 are repeated until said disease risk level in claim 12 is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke.~~

Claim 18 (Currently amended): A method as in claim 1 wherein ~~said method in claim 2 through said method in claim 16 all the methods in said all processes in claim 1 are written as an executable computer program named said MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said methods and to~~

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output a result of said methods to a display or a memory or another computer on a network, or to a user comprising:

starting the MMA.exe program on said device;

inputting the currently measured values, the previously measured values and the normal values of the individual's atherosclerosis parameters into the input screen of said MMA.exe by using the keyboard of said device;

clicking the "update" button and the "calc. risk" button of said input screen;

clicking the "evaluate" button of the MMA.exe output screen; and

outputting said output screen to a display or a memory or another computer on a network, or to a user by said computer device so as to produce a result of said methods, called the screening report containing a total risk of said disease, a disease risk level, a primary cause in said disease, a primary therapy target of said disease, a secondary therapy target of said disease and a therapeutic efficiency, to an

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individual who requires the diagnosis, the prevention or the treatment of atherosclerosis-related CHD or stroke.